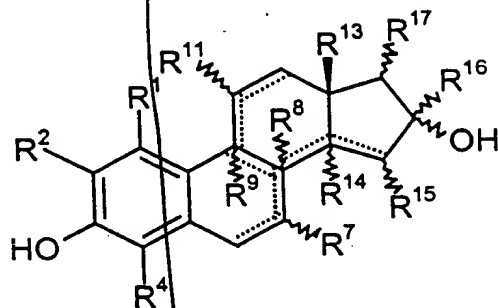


Claims

1. 3,16-Dihydroxyestra-1,3,5(10)-triene derivatives of general formula I



(I)

in which radicals R^1 to R^{17} , independently of one another, have the following meanings:

- R^1 means a halogen atom, a hydroxyl group, a methyl group, a trifluoromethyl group, a methoxy group, an ethoxy group or a hydrogen atom;
- R^2 means a halogen atom, a hydroxyl group, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or a hydrogen atom;
- R^4 means a halogen atom, a straight-chain or branched-chain, saturated or unsaturated alkyl group with up to 10 carbon atoms, a trifluoromethyl or pentafluoroethyl group, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or a hydrogen atom;

- 5 R⁷ means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms, an optionally substituted aryl or heteroaryl radical or a hydrogen atom;
- 10 R⁸ means a hydrogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position or a cyano group in α - or β -position;
- 15 R⁹ means a hydrogen atom in α - or β -position, a methyl, ethyl, trifluoromethyl or pentafluoroethyl group in α - or β -position;
- 20 R¹¹ means a nitrooxy group in α - or β -position, a hydroxyl or mercapto group in α - or β -position, a halogen atom in α - or β -position, a chloromethyl group in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a
- 25 straight-chain or branched-chain, saturated or unsaturated alkoxy or alkylthio group with up to 6 carbon atoms, an optionally substituted aryl or heteroaryl radical or a hydrogen atom;

R¹³ means a methyl, ethyl, trifluoromethyl or pentafluoroethyl group in β -position;

and either

R¹⁴ means a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position or a hydrogen atom in α - or β -position

and

R¹⁵ means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position that can be interrupted by one or more oxygen atoms, sulfur atoms, sulfoxide or sulfone groups or imino groups = NR^{15'} (R^{15'} = hydrogen atom, methyl, ethyl, propyl, i-propyl) or a hydrogen atom

or

R¹⁴ and R¹⁵ together mean a 14 α ,15 α -methylene or 14 β ,15 β -methylene group that is optionally substituted with one or two halogen atoms;

R¹⁶ means a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a trifluoromethyl or pentafluoroethyl group, a cyanomethyl group or a hydrogen atom in α - or β -position;

R¹⁷ means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a hydrogen atom or a hydroxyl group

and the dotted lines ----- in rings B, C and D optionally mean one or more double bonds, and the wavy lines

mean the arrangement of the respective substituent in α - or β -position,

excluding the compounds *estra-1,3,5(10)-triene-3,16 α -diol*, *estra-1,3,5(10)-triene-3,16 β -diol*, *estra-1,3,5(10),7-tetraene-3,16 α -diol* and *estra-1,3,5(10),7-tetraene-3,16 β -diol*.

2. Compounds according to claim 1, in which radicals R¹ to R¹⁷, independently of one another, have the following meanings

R¹ means a fluorine atom, a hydroxyl group, a methyl group, a trifluoromethyl group, a methoxy group, an ethoxy group or a hydrogen atom;

R² means a fluorine atom, a hydroxyl group, a methoxy or ethoxy group or a hydrogen atom;

R⁴ means a fluorine atom, a methyl, ethyl, trifluoromethyl, methoxy or ethoxy group or a hydrogen atom;

R⁷ means a fluorine atom in α - or β -position, a methyl, ethyl, propyl or i-propyl group in α - or β -position,

an optionally substituted aryl radical, a trifluoromethyl group in α - or β -position or a hydrogen atom;

5 R^8 means a hydrogen atom in α - or β -position, a methyl or ethyl group in α - or β -position;

R^9 means a hydrogen atom in α - or β -position, a methyl, ethyl, trifluoromethyl or pentafluoroethyl group in α - or β -position;

10 R^{11} means a nitrooxy group in α - or β -position, a hydroxyl group in α - or β -position, a fluorine atom in α - or β -position, a chloromethyl group in α - or β -position, a methyl group in α - or β -position, a methoxy group in α - or β -position, a phenyl- or 3-methylthien-2-yl radical in α - or β -position or a hydrogen atom;

15 R^{13} means a methyl or ethyl group in β -position;

and either

R^{14} means a hydrogen atom in α - or β -position or a methyl group in α - or β -position

20 and

R^{15} means a fluorine atom in α - or β -position, a methyl group in α - or β -position, or a hydrogen atom,

or

25 R^{14} and R^{15} together mean a $14\alpha,15\alpha$ -methylene group or a $14\beta,15\beta$ -methylene group

R^{16} means a methyl, ethyl, ethinyl, propinyl or trifluoromethyl group;

R^{17} means a fluorine atom in α - or β -position, a methyl group, a hydrogen atom or a hydroxyl group,

and the dotted lines ----- in rings B, C and D optionally mean an additional double bond between carbon atoms 9 and 11.

3. Compounds of general formula I according to claim 1, in which

R⁷ means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms, or an optionally substituted aryl or heteroaryl radical

and

R¹, R², R⁴, R⁸, R⁹, R¹¹, R¹⁴, R¹⁵, R¹⁶ and R¹⁷ in each case mean a hydrogen atom.

4. Compounds of general formula I according to claim 1, in which

R¹¹ means a nitrooxy group in α - or β -position, a hydroxyl or mercapto group in α - or β -position, a halogen atom in α - or β -position, a chloromethyl group in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy or alkylthio group with up to 6 carbon atoms, or an optionally substituted aryl or heteroaryl radical, and

R^1 , R^2 , R^4 , R^7 , R^8 , R^9 , R^{14} , R^{15} , R^{16} and R^{17} in each case mean a hydrogen atom.

5. Compounds of general formula I according to claim 1, in which

R^{15} means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position that can be interrupted by one or more oxygen atoms, sulfur atoms, sulfoxide or sulfone groups or imino groups = $NR^{15'}$ ($R^{15'}$ = hydrogen atom, methyl, ethyl, propyl, *i*-propyl), and

R^1 , R^2 , R^4 , R^7 , R^8 , R^9 , R^{11} , R^{14} , R^{16} and R^{17} in each case mean a hydrogen atom.

6. Compounds of general formula I according to claim 1, in which

R^7 means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or an optionally substituted aryl or heteroaryl radical,

R^{11} means a nitrooxy group in α - or β -position, a hydroxyl or mercapto group in α - or β -position, a halogen atom in α - or β -position, a chloromethyl group in α - or β -position, a straight-chain or

004030 T 63460

branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy or alkylthio group with up to 6 carbon atoms or an optionally substituted aryl or heteroaryl radical, and

R^1 , R^2 , R^4 , R^8 , R^9 , R^{14} , R^{15} , R^{16} and R^{17} in each case mean a hydrogen atom.

7. Compounds of general formula I according to claim 1, in which

R^7 means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or an optionally substituted aryl or heteroaryl radical,

R^{15} means a halogen atom in α - or β -position or a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position that can be interrupted by one or more oxygen atoms, sulfur atoms, sulfoxide or sulfone groups or imino groups = $NR^{15'}$ ($R^{15'}$ = hydrogen atom, methyl, ethyl, propyl, i-propyl), and

004420 T 654650

R^1 , R^2 , R^4 , R^8 , R^9 , R^{11} , R^{14} , R^{16} and R^{17} in each case mean a hydrogen atom.

8. Compounds of general formula I according to claim 1, in which

R^{11} means a nitrooxy group in α - or β -position, a hydroxy or mercapto group in α - or β -position, a halogen atom in α - or β -position, a chloromethyl group in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy or alkylthio group with up to 6 carbon atoms or an optionally substituted aryl or heteroaryl radical,

R^{15} means a halogen atom in α - or β -position or a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position that can be interrupted by one or more oxygen atoms, sulfur atoms, sulfoxide or sulfone groups or imino groups = $NR^{15'}$ ($R^{15'}$ = hydrogen atom, methyl, ethyl, propyl, i-propyl), and

R^1 , R^2 , R^4 , R^7 , R^8 , R^9 , R^{14} , R^{16} , and R^{17} in each case mean a hydrogen atom.

9. Compounds of general formula I according to claim 1, in which

R⁷ means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or an optionally substituted aryl or heteroaryl radical,

R¹¹ means a nitrooxy group in α - or β -position, a hydroxyl or mercapto group in α - or β -position, a halogen atom in α - or β -position, a chloromethyl group in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy or alkylthio group with up to 6 carbon atoms or an optionally substituted aryl or heteroaryl radical,

R¹⁵ means a halogen atom in α - or β -position, or a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position that can be interrupted by one or more oxygen atoms, sulfur atoms, sulfoxide or sulfone groups or imino groups = NR^{15'} (R^{15'} = hydrogen atom, methyl, ethyl, propyl, i-propyl), and

R^1 , R^2 , R^4 , R^8 , R^9 , R^{14} , R^{16} and R^{17} in each case mean a hydrogen atom.

10. Compounds according to claim 1, characterized in that the dotted lines mean one or more conjugated double bonds.

11. Compounds according to claim 1, wherein there is a double bond between C atoms 6 and 7.

12. Compounds according to claim 1, wherein there is a double bond between C atoms 7 and 8.

13. Compounds according to claim 1, wherein there is a double bond between C atoms 8 and 9.

14. Compounds according to claim 1, wherein there is a double bond between C atoms 9 and 11.

15. Compounds according to claim 1, wherein there is a double bond between C atoms 8 and 14.

16. Compounds according to claim 1, wherein there is a double bond between C atoms 11 and 12.

17. Compounds according to claim 1, wherein there is a double bond between C atoms 14 and 15.

18. Compounds according to claim 10, wherein there are double bonds between C atoms 6 and 7 and C atoms 8 and 9.

19. Compounds according to claim 10, wherein there are double bonds between C atoms 8 and 9 and C atoms 14 and 15.

20. Compounds according to claim 10, wherein there are double bonds between C atoms 6 and 7, C atoms 8 and 9 and C atoms 11 and 12.

21. Compounds according to claim 10, wherein there are double bonds between C atoms 6 and 7, C atoms 8 and 9 and C atoms 14 and 15.

004020-15925450

22. Compounds according to claim 10, wherein there are double bonds between C atoms 6 and 7, C atoms 8 and 9, C atoms 11 and 12 and C atoms 14 and 15.

23. Compounds according to ~~one of claims 1 to 22,~~ *claim 1* wherein one or both hydroxyl groups is (are) esterified at C atoms 3 and 16 with an aliphatic or aromatic carboxylic acid or with an α - or β -amino acid.

24. Compounds according to claim 1, namely
 14 α ,15 α -Methylen-estra-1,3,5(10)-triene-3,16 α -diol
 14 β ,15 β -Methylen-estra-1,3,5(10)-triene-3,16 α -diol
 14 β ,15 β -Methylen-estra-1,3,5(10),8(9)-tetraene-3,16 α -
 5 diol,

Estra-1,3,5(10),8(9)-tetraene-3,16 α -diol,

Estra-1,3,5(10),8(14)-tetraene-3,16 α -diol,

Estra-1,3,5(10),6,8-pentaene-3,16 α -diol,

7 α -Fluoro-estra-1,3,5(10)-triene-3,16 α -diol,

11 β -Methoxy-estra-1,3,5(10)-triene-3,16 α -diol,

7 α -Methyl-estra-1,3,5(10)-triene-3,16 α -diol

11 β -Fluoro-estra-1,3,5(10)-triene-3,16 α -diol,

8 α -Estra-1,3,5(10)-triene-3,16 α -diol

Estra-1,3,5(10)-triene-2,3,16 α -triol

15 17 β -Fluoro-estra-1,3,5(10)-triene-3,16 α -diol,

18a-Homo-estra-1,3,5(10)-triene-3,16 α -diol,

18a-Homo-estra-1,3,5(10),8(9)-tetraene-3,16 α -diol,

18a-Homo-14 α ,15 α -methylen-estra-1,3,5(10)-triene-3,16 α -
 diol,

20 18a-Homo-14 α ,15 α -methylen-estra-1,3,5(10),8(9)-tetraene-
 3,16 α -diol,

004020 T68/6450

7 α -Phenyl-estra-1,3,5(10)-triene-3,16 α -diol
7 α -Methoxy-estra-1,3,5(10)-triene-3,16 α -diol
7 α -Thiomethyl-estra-1,3,5(10)-triene-3,16 α -diol
7 α -Cyanomethyl-estra-1,3,5(10)-triene-3,16 α -diol
5 7 β -Ethyl-estra-1,3,5(10)-triene-3,16 α -diol
7 β -Propyl-estra-1,3,5(10)-triene-3,16 α -diol
7 β -i-Propyl-estra-1,3,5(10)-triene-3,16 α -diol
7 β -i-Propenyl-estra-1,3,5(10)-triene-3,16 α -diol
7 β -Phenyl-estra-1,3,5(10)-triene-3,16 α -diol
10 7 β -Methoxy-estra-1,3,5(10)-triene-3,16 α -diol
7 β -Thiomethyl-estra-1,3,5(10)-triene-3,16 α -diol
7 β -Cyanomethyl-estra-1,3,5(10)-triene-3,16 α -diol
7 α -Ethyl-estra-1,3,5(10)-triene-3,16 β -diol
7 α -Propyl-estra-1,3,5(10)-triene-3,16 β -diol
15 7 α -i-Propyl-estra-1,3,5(10)-triene-3,16 β -diol
7 α -i-Propenyl-estra-1,3,5(10)-triene-3,16 β -diol
7 α -Phenyl-estra-1,3,5(10)-triene-3,16 β -diol
7 α -Methoxy-estra-1,3,5(10)-triene-3,16 β -diol
7 α -Thiomethyl-estra-1,3,5(10)-triene-3,16 β -diol
20 7 α -Cyanomethyl-estra-1,3,5(10)-triene-3,16 β -diol
7 β -Ethyl-estra-1,3,5(10)-triene-3,16 β -diol
7 β -Propyl-estra-1,3,5(10)-triene-3,16 β -diol
7 β -i-Propyl-estra-1,3,5(10)-triene-3,16 β -diol
7 β -i-Propenyl-estra-1,3,5(10)-triene-3,16 β -diol
25 7 β -Phenyl-estra-1,3,5(10)-triene-3,16 β -diol
7 β -Methoxy-estra-1,3,5(10)-triene-3,16 β -diol
7 β -Thiomethyl-estra-1,3,5(10)-triene-3,16 β -diol

004030 T69460

5

15 α -Ethyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -Allyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -i-Propyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -i-Propenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -Methoxy-estra-1,3,5(10)-triene-3,16 α -diol

15 α -Thiomethyl-estra-1,3,5(10)-triene-3,16 α -diol

10 15 α -Methyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Ethyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Propyl-estra-1,3,5(10)-triene- β ,16 β -diol

15 α -Allyl-estra-1,3,5(10)-triene-3,16 β -diol

~~15 α -i-Propyl-estra-1,3,5(10)-triene-3,16 β -diol~~

15 15 α -**i**-Propenyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Methoxy-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Thiomethyl-estra-1,3,5(10')-triene-3,16 β -diol

15 β -Methyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Ethyl-estra-1,3,5(10)-triene-3,16 α -diol

20 15 β -Propyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Allyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -1-Propyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -i-Propenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Methoxy-estra-1,3,5(10)-triene-3,16 α -diol

25 15 β -Thiomethyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Methyl-estra-1,3,5(10)-triene-3,16 β -diol

15 β -Ethyl-estra-1,3,5(10)-triene-3,16 β -diol

15 β -Propyl-estra-1,3,5(10)-triene-3,16 β -diol

15 β -Allyl-estra-1,3,5(10)-triene-3,16 β -diol

15 β -i-Propyl-estra-1,3,5(10)-triene-3,16 β -diol

15 β -i-Propenyl-estra-1,3,5(10)-triene-3,16 β -diol

5 15 β -Methoxy-estra-1,3,5(10)-triene-3,16 β -diol

15 β -Thiomethyl-estra-1,3,5(10)-triene-3,16 β -diol

7 α -Trifluoromethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

10 7 α -Pentafluoroethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 α -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 α -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 α -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

15 7 α -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 α -Phenyl-11 β -Fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 α -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 α -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

20 7 α -Cyanomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 β -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 β -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 β -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

25 7 β -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 β -Phenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

7 β -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
 7 β -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -
 diol
 7 β -Cyanomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -
 5 diol
 7 α -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 α -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 α -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 α -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
 10 diol
 7 α -Phenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 α -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 α -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
 diol
 7 α -Cyanomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
 15 diol
 7 β -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 β -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 β -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 20 7 β -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
 diol
 7 β -Phenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 β -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
 7 β -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
 25 diol
 7 β -Cyanomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
 diol
 15 α -Methyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

0049394 02400

15 α -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 α -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 α -Allyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 α -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
5 15 α -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -
diol
15 α -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 α -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -
diol
10 15 α -Methyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
15 α -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
15 α -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
15 α -Allyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
15 α -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
15 15 α -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
diol
15 α -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol
15 α -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -
diol
20 15 β -Methyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 β -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 β -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 β -Allyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
15 β -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol
25 15 β -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -
diol
15 β -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

09497891 020450

15 β -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Methyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

15 β -Ethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

5 15 β -Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

15 β -Allyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

15 β -i-Propyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

15 β -i-Propenyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

10 15 β -Methoxy-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

15 β -Thiomethyl-11 β -fluoro-estra-1,3,5(10)-triene-3,16 β -diol

14 α ,15 α -Methylene-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 14 β ,15 β -Methylene-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

14 β ,15 β -Methylene-7 α -phenyl-estra-1,3,5(10),8(9)-tetraene-3,16 α -diol,

7 α -Phenyl-estra-1,3,5(10),8(9)-tetraene-3,16 α -diol,

20 7 α -Phenyl-estra-1,3,5(10),8(14)-tetraene-3,16 α -diol,

7 α -Phenyl-estra-1,3,5(10),6,8-pentaene-3,16 α -diol,

11 β -Methoxy-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol,

11 β -Fluoro-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol,

7 α -Phenyl-8 α -estra-1,3,5(10)-triene-3,16 α -diol

25 7 α -Phenyl-estra-1,3,5(10)-triene-2,3,16 α -triol

17 β -Fluoro-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol,

18a-Homo-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol,

18a-Homo-7 α -phenyl-estra-1,3,5(10),8(9)-tetraene-3,16 α -diol,

18a-Homo-14 α ,15 α -methylene-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol,

5 18a-Homo-14 α ,15 α -methylene-7 α -phenyl-estra-1,3,5(10),8(9)-tetraene-3,16 α -diol,

18a-Homo-14 α ,15 α -methylene-7 α -phenyl-estra-1,3,5(10),6,8-pentaene-3,16 α -diol,

10 14 α ,15 α -Methylene-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

14 β ,15 β -Methylene-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

14 β ,15 β -Methylene-7 α -phenyl-estra-1,3,5(10),8(9)-tetraene-3,16 β -diol,

15 7 α -Phenyl-estra-1,3,5(10),8(9)-tetraene-3,16 β -diol,

7 α -Phenyl-estra-1,3,5(10),8(14)-tetraene-3,16 β -diol,

7 α -Phenyl-estra-1,3,5(10),6,8-pentaene-3,16 β -diol,

11 β -Methoxy-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol,

11 β -Fluoro-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol,

20 7 α -Phenyl-8 α -estra-1,3,5(10)-triene-3,16 β -diol

7 α -Phenyl-estra-1,3,5(10)-triene-2,3,16 α -triol

17 β -Fluoro-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol,

18a-Homo-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol,

25 18a-Homo-7 α -phenyl-estra-1,3,5(10),8(9)-tetraene-3,16 β -diol,

18a-Homo-14 α ,15 α -methylene-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol,

004030 T6026460

18a-Homo-14 α ,15 α -methylene-7 α -phenyl-estra-
1,3,5(10),8(9)-tetraene-3,16 β -diol,

18a-Homo-14 α ,15 α -methylene-7 α -phenyl-estra-1,3,5(10),6,8-
pentaene-3,16 β -diol,

5 15 α -Methyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -Ethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -Allyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -i-Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

10 15 α -i-Propenyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -
diol

15 α -Methoxy-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 α -Thiomethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -
diol

15 15 α -Methyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Ethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Allyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -i-Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

20 15 α -i-Propenyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -
diol

15 α -Methoxy-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol

15 α -Thiomethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -
diol

25 15 β -Methyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Ethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -Allyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol

15 β -i-Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol
15 β -i-Propenyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -
diol
15 β -Methoxy-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -diol
5 15 β -Thiomethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 α -
diol
15 β -Methyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol
15 β -Ethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol
15 β -Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol
10 15 β -Allyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol
15 β -i-Propyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol
15 β -i-Propenyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -
diol
15 β -Methoxy-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -diol
15 15 β -Thiomethyl-7 α -phenyl-estra-1,3,5(10)-triene-3,16 β -
diol
15 α -Methyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol
15 α -Ethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
20 3,16 α -diol
15 α -Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol
15 α -Allyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol
25 15 α -i-Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

004030-1-004030

15 α -i-Propenyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 α -diol

15 α -Methoxy-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

5 15 α -Thiomethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 α -diol

15 α -Methyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

10 15 α -Ethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 α -Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 α -Allyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -
-diol

15 α -i-Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 α -i-Propenyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 β -diol

20 15 α -Methoxy-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 α -Thiomethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 β -diol

25 15 β -Methyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

15 β -Ethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

004020" T6046460

15 β -Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

15 β -Allyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

5 15 β -i-Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

15 β -i-Propenyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 α -diol

15 β -Methoxy-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 α -diol

15 β -Thiomethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 α -diol

15 β -Methyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 β -Ethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 β -Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

20 15 β -Allyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 β -i-Propyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 β -i-Propenyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 β -diol

25 15 β -Methoxy-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-triene-
3,16 β -diol

15 β -Thiomethyl-11 β -fluoro-7 α -phenyl-estra-1,3,5(10)-
triene-3,16 β -diol

004939-76926469

11 β -[2-(3-Methylthien)-yl]-estra-1,3,5(10)-triene-3,16 α -diol

11 β -[2-(3-Methylthien)-yl]-estra-1,3,5(10)-triene-3,16 β -diol.

25. Compounds according to claim 24, namely

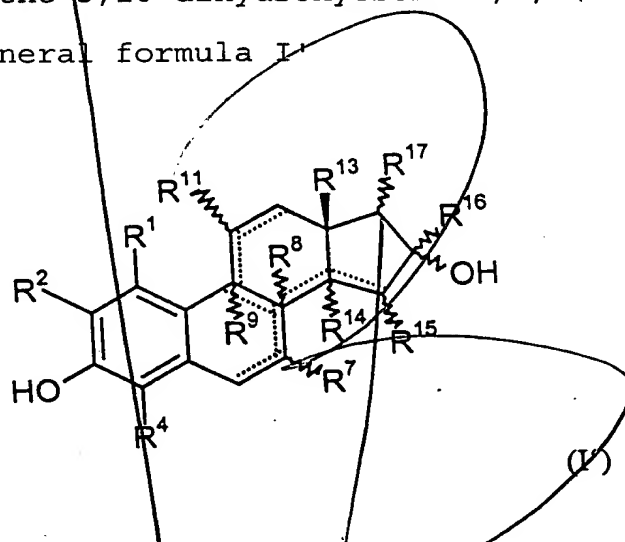
7 α -Fluoro-estra-1,3,5(10)-triene-3,16 α -diol,

7 α -Methyl-estra-1,3,5(10)-triene-3,16 β -diol

7 α -Methyl-estra-1,3,5(10)-triene-3,16 α -diol

18 α -Homo-estra-1,3,5(10)-triene-3,16 α -diol.

26. Use of the 3,16-dihydroxyestra-1,3,5(10)-triene derivatives of general formula I



in which radicals R^1 to R^{17} , independently of one another, have the following meanings

R^1 means a halogen atom, a hydroxyl group, a methyl group, a trifluoromethyl group, a methoxy group, an ethoxy group or a hydrogen atom;

R^2 means a halogen atom, a hydroxyl group, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or a hydrogen atom;

- 5
10
15
20
25
- R^4 means a halogen atom, a straight-chain or branched-chain, saturated or unsaturated alkyl group with up to 10 carbon atoms, a trifluoromethyl or pentafluoroethyl group, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or a hydrogen atom;
- R^7 means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms, an optionally substituted aryl or heteroaryl radical or a hydrogen atom;
- R^8 means a hydrogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position or a cyano group in α - or β -position;
- R^9 means a hydrogen atom in α - or β -position, a methyl, ethyl, trifluoromethyl or pentafluoroethyl group in α - or β -position;
- R^{11} means a nitrooxy group in α - or β -position, a hydroxyl or mercapto group in α - or β -position, a halogen atom in α - or β -position, a chloromethyl group in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with

up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy or alkylthio group with up to 6 carbon atoms, an optionally substituted aryl or heteroaryl radical or a hydrogen atom;

R^{13} means a methyl, ethyl, trifluoromethyl or pentafluoroethyl group in β -position;

and either

R^{14} means a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position or a hydrogen atom in α - or β -position

and

R^{15} means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position that can be interrupted by one or more oxygen atoms, sulfur atoms, sulfoxide or sulfone groups or imino groups = $NR^{15'}$ ($R^{15'}$ = hydrogen atom, methyl, ethyl, propyl, i-propyl) or a hydrogen atom

or

R^{14} and R^{15} together mean a $14\alpha,15\alpha$ -methylene or $14\beta,15\beta$ -methylene group that is optionally substituted with one or two halogen atoms;

R¹⁶ means a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a trifluoromethyl or pentafluoroethyl group, a cyanomethyl group or a hydrogen atom in α - or β -position;

R¹⁷ means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a hydrogen atom or a hydroxyl group

and the dotted lines ----- in rings B, C and D optionally mean one or more double bonds, and the wavy lines mean the arrangement of the respective substituent in α - or β -position, for treatment of estrogen-deficiency-induced diseases and conditions in women and in men.

27. Use according to claim 26 for the treatment of peri- and post-menopausal symptoms.

28. Use according to claim 26 for treatment of peri- and post-male-menopausal symptoms.

29. Use according to claim 27 for prevention and treatment of hot flashes, sleep disturbances, irritability, mood swings, incontinence, vaginal atrophy, and hormone-deficiency-induced emotional diseases.

30. Use according to claim 29 for prevention and treatment of diseases in the urogenital tract.

31. Use according to claim 26 for prevention and therapy of gastrointestinal diseases.

32. Use according to claim 31 for prevention and therapy of ulcers and hemorrhagic diatheses in the gastrointestinal tract.

33. Use according to claim 32 for prevention and therapy of neoplasias.

34. Use according to claim 26 for in-vitro treatment of male infertility.

35. Use according to claim 26 for in-vivo treatment of male infertility.

36. Use according to claim 26 for in-vitro treatment of female infertility.

37. Use according to claim 26 for in-vivo treatment of female infertility.

38. Use according to claim 26 for hormone replacement therapy (HRT).

39. Use according to claim 26 for the therapy of hormone-deficiency-induced symptoms in the case of surgical, medicinal or ovarian dysfunction that is caused in some other way.

40. Use according to claim 26 for prophylaxis and therapy of a hormone-deficiency-induced bone mass loss.

41. Use according to claim 40 for prophylaxis and therapy of osteoporosis.

42. Use according to claim 26 for prevention and therapy of cardiovascular diseases.

43. Use according to claim 26 for prevention and treatment of vascular diseases.

004930" T5945460

44. Use according to claim 43 for prevention and treatment of arteriosclerosis.

45. Use according to claim 43 for prevention and treatment of neointimal hyperplasias.

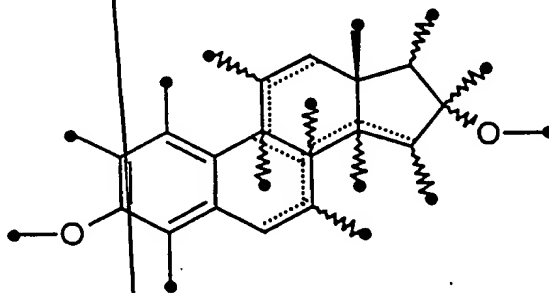
46. Use according to claim 26 for prevention and treatment of hormone-deficiency-induced neurodegenerative diseases.

47. Use according to claim 26 for prevention and treatment of Alzheimer's disease and hormone-deficiency-induced impairment of memory and learning capacity.

48. Use according to claim 26 for treatment of inflammatory diseases and diseases of the immune system.

49. Use according to claim 26 for prevention and treatment of benign prostate hyperplasia (BPH).

50. Use of the structural part of formula II

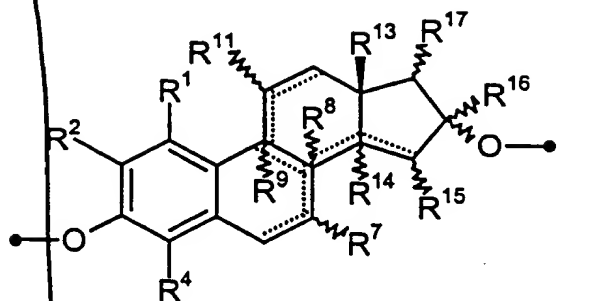


(II)

as a component of the total structure of compounds that have a dissociation in favor of their estrogenic action on bone rather than the uterus.

004020 T6845459

51. Use of the structural part of general formula 'II'
according to claim 50



(II')

in which radicals R¹ to R¹⁷, independently of one another,
have the following meanings

- R¹ means a halogen atom, a hydroxyl group, a methyl group, a trifluoromethyl group, a methoxy group, an ethoxy group or a hydrogen atom;
- R² means a halogen atom, a hydroxyl group, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or a hydrogen atom;
- R⁴ means a halogen atom, a straight-chain or branched-chain, saturated or unsaturated alkyl group with up to 10 carbon atoms, a trifluoromethyl or pentafluoroethyl group, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms or a hydrogen atom;

- 5 R^{7'} means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated alkoxy group with up to 6 carbon atoms, an optionally substituted aryl or heteroaryl radical or a hydrogen atom;
- 10 R^{8'} means a hydrogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position or a cyano group in α - or β -position;
- 15 R^{9'} means a hydrogen atom in α - or β -position, a methyl, ethyl, trifluoromethyl or pentafluoroethyl group in α - or β -position;
- 20 R^{11'} means a nitrooxy group in α - or β -position, a hydroxyl or mercapto group in α - or β -position, a halogen atom in α - or β -position, a chloromethyl group in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a
- 25 straight-chain or branched-chain, saturated or unsaturated alkoxy or alkylthio group with up to 6 carbon atoms, an optionally substituted aryl or heteroaryl radical or a hydrogen atom;

R^{13'} means a methyl, ethyl, trifluoromethyl or pentafluoroethyl group in β -position;

and either

R^{14'} means a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position or a hydrogen atom in α - or β -position

and

R^{15'} means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position that can be interrupted by one or more oxygen atoms, sulfur atoms, sulfoxide or sulfone groups or imino groups = NR^{15'} (R^{15'} = hydrogen atom, methyl, ethyl, propyl, i-propyl) or a hydrogen atom

or

R^{14'} and R^{15'} together mean a 14 α ,15 α -methylene group or a 14 β ,15 β -methylene group that is optionally substituted with one or two halogen atoms;

R^{16'} means a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a trifluoromethyl or pentafluoroethyl group, a cyanomethyl group or a hydrogen atom in α - or β -position;

R^{17'} means a halogen atom in α - or β -position, a straight-chain or branched-chain, saturated or unsaturated, optionally partially or completely fluorinated alkyl group with up to 10 carbon atoms in α - or β -position, a hydrogen atom or a hydroxyl group,

and the dotted lines ---- in rings B, C and D optionally mean one or more double bonds, and the wavy lines mean the arrangement of the respective substituents in α - or β -position.

52. Pharmaceutical compositions that contain at least one compound according to ^{claim 1} ~~one of claims 1 to 25~~ as well as a pharmaceutically compatible vehicle.

Add
B1

0044020" T6926450